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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,641	10/27/2003	Deanna L. Kroetz	02307O-115611US	4011

20350 7590 12/29/2005

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/694,641	KROETZ ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/694641*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-41* is/are pending in the application.

4a) Of the above claim(s) *19-20 and 35-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-18,21-23,26-34 and 37-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

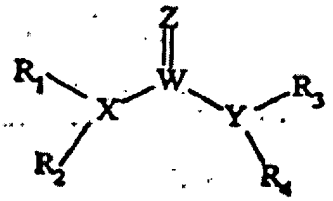
Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/15/05/ 10/27/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

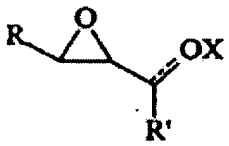
1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 15-18 and 31-34, drawn to a method for reducing blood pressure or hypertension comprising administering a compound represented by the



formula , classified in class 514, subclass 476-482.

II. Claims 19-20 and 35-36, drawn to a method for reducing blood pressure or hypertension comprising administering a compound represented by the formula



, classified in class 514, subclass 529.

It is noted that claims 14, 21-23, 26-30, 37-41 will be examined to the extent that they read on the elected formula because they contain common limitations for Group I and Group II.

Because these inventions I and II are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

2. In addition, applicant is required under 35 U.S.C. 121 to elect a single disclosed species under the instant claims of the elected Group. Moreover, whatever specific compound is ultimately elected, applicants are required to list all claims readable thereon.

With the election of a specific exemplified compound, a generic concept will be identified by the examiner as the inventive group for examination.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

3. During a telephone conversation with Laurence J. Hyman on December 07, 2005 a provisional election was made to prosecute the invention of Group I Invention along with the subgenus compounds (Z=O, W=C, X and Y= N, R2 and R4=H) as the elected species. Claims 14-18, 21-23, 26-29 and 30-34 read on the elected invention. Affirmation of this election must be made by applicant in replying to this Office action. Claims 19-20 and 35-36 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

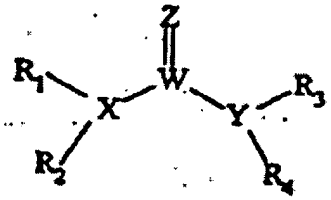
The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 14, 21-23, 26-30 and 37-41 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The present claim is drawn to a method of reducing blood pressure or hypertension in a patient comprising administering an inhibitor of soluble epoxide hydrolase.

The instant specification provides assays to test the compounds in vitro and discloses that the compounds exhibit epoxide hydrolase activity. The instant specification discloses a



compound of , namely N-cyclohexyl-N'-dodecylurea, N-cyclohexyol-N'-ethylurea and dodecylamine as an example of soluble epoxide hydrolase inhibitor, and tested for their efficacy in decreasing blood pressure in rat (Figures 4-5 and Example).

As discussed above, the specification is based on studies regarding the activity of N-cyclohexyl-N'-dodecylurea, N-cyclohexyol-N'-ethylurea and dodecylamine in decreasing blood pressure in rat, which meets the written description. However, the claims are directed to

encompass any "soluble epoxide hydrolase inhibitor", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. None of these meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of N-cyclohexyl-N'-dodecylurea, N-cyclohexyol-N'-ethylurea and dodecylamine (more broadly compounds of the structure having Z=O, W=C, X and Y= N, R2 and R4=H substituents), the skilled artisan cannot envision which "soluble epoxide hydrolase inhibitor" would have similar activity as the tested compounds. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

6. Claims 14-18, 21-23, 26-34 and 37-41 are rejected under 35 USC 112, first paragraph, because the specification while being enabling for the claimed utility of the specific soluble epoxide hydrolase inhibitor such as N-cyclohexyl-N'-dodecylurea, N-cyclohexyol-N'-ethylurea and dodecylamine (more broadly compounds of the structure having Z=O, W=C, X and Y= N, R2 and R4=H substituents), does not reasonably provide enablement for the an inhibitor of soluble epoxide hydrolase, a compound represented by the formula, or other subgenus of compounds represented by the formula (for example Z=sulfur, W=phosphorus or sulfur, Y=oxygen or sulfur). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d

1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; the breadth of the claims; the amount of direction or guidance presented; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

As discussed above, the present claim is drawn to a method of reducing blood pressure or hypertension in a patient comprising administering an inhibitor of soluble epoxide hydrolase.

Compounds of the formula are generally recognized in the art as having different activity depending upon different substituents at Z, W, X and Y. For example, the activity of derivatives of ureas significantly differs from the activity of organophosphorus or organophosphate compounds. The relative skill or unpredictability of those in the art of pharmaceuticals is high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instantly claimed compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation.

The breadth of the instant claims covers plethora of compounds (over 1000 compounds) that may not necessarily share same core groups.

In the instant case, compounds of N-cyclohexyl-N'-dodecylurea, N-cyclohexyol-N'-ethylurea and dodecylamine are disclosed as working examples and tested for its efficacy in decreasing blood pressure. As discussed above, very limited numbers of the compounds are set forth as working examples in the instant specification. The specification provides no guidance, in the way of enablement for the full scope of all compounds that are potentially suitable for the invention work similarly as to the tested compounds. The skill artisan would have not known that which compounds of the claimed compounds are capable of accomplishing the desired result of the claimed invention **without undue amount of experimentation**.

Since the efficacy of said compounds in increasing erythropoietin mentioned above cannot be predicted from a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claims 14-18, 21-22, 30-34 and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Ichihara et al. (JP 07304755).

Ichihara teaches use of compounds represented by the instant formula (e.g., RN 174398-90-4, RN 174398-91-5, RN 174398-92-6, RN 174398-93-7, etc...) or their salt for the treatment of cardiovascular disease such as hypertension by modulating rennin-angiotenisn system, wherein said compound is administered in various dosage forms including oral dosage forms (i.e., tablet, capsule). Ichihara discloses that a rennin inhibitor tends to control generation of angiotensin II which works powerfully to pressure ups, such as a vasoconstrictor action and aldosterone secretion, by checking the reaction of the rennin and rennin substrate (angiotensiongen) which are called rate-determining step of the rening-angiogensin series which is a pressure-up system in the living body, and reducing generation of angiotensin I).

Although Ichihara is silent about the functional characteristic of said compounds in inhibiting soluble epoxide hydrolase, such property or characteristic deems to be inherent to the compounds disclosed by Ichihara which read on the claimed structure compounds. Thus, Ichihara anticipates the claimed invention.

8. Claims 14-18, 21-23, 27-34 and 37-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Blum et al. (US 5962455).

Blum teaches use of compounds represented by the instant formula (e.g., RN 202472-67-1, RN 202472-68-2, RN 202472-69-3, RN 202472-70-6,etc...) or their salt for the treatment of cardiovascular disease including hypertension or essential hypertension as well as congestive heart failure, wherein said compound is administered in dosage amounts of from about 0.1mg to about 140mg per kilograms of body weight per day and in various dosage forms including oral dosage form (abstract; column 8, line 52 thru column 10, line 62).

Although Blum is silent about the functional characteristic of said compounds in inhibiting soluble epoxide hydrolase, such property or characteristic deems to be inherent to the compounds disclosed by Blum which read on the claimed structure compounds. Thus, Blum anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 26 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blum et al. (US 5962455), and further in view of The Merck Manual ("Hypertension", Fifteenth Edition, 1987).

The teaching Blum has been discussed in above 35 USC 102(e) rejection.

The teaching of Blum differs from the claimed invention in the use of said compounds in reducing systolic blood pressure.

As discussed above, the prior art does not specifically disclose the instantly claimed utility in patients with systolic blood pressure. However, one having ordinary skill in the art would have expected at the time of the invention was made that the application to patient having systolic high blood pressure would have been characteristic of the prior art method. Since the prior art does not distinguish the utility of known anti-hypertensive medications for only systolic blood pressure management, the skilled artisan would have expected that the Blum's compounds

having antihypertensive effect would provide benefit for the patient having systolic blood pressure.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

10. Claims 30-34 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-5 of prior U.S. Patent No. 6,531,506. This is a double patenting rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 14-18, 21-23, 26-34 and 37-41 are rejected under the judicially created doctrine of double patenting over claims 6-9 of U. S. Patent No. 6,531,506.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the both of the instant application and the patent are directed to the therapeutic treatment of hypertension with same compounds. The scope of the claimed invention overlaps with the patent.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614